ACTA2 gene

actin, alpha 2, smooth muscle, aorta

Normal Function

The *ACTA2* gene provides instructions for making a protein called smooth muscle alpha (α)-2 actin, which is part of the actin protein family. Actin proteins are important for cell movement and the tensing (contraction) of muscles.

Smooth muscle α-2 actin is found in smooth muscle cells. Smooth muscles line the internal organs, including the blood vessels, stomach, and intestines. Within smooth muscle cells, smooth muscle α-2 actin forms the core of structures called sarcomeres, which are necessary for muscles to contract. Smooth muscles contract and relax as part of their normal function without being consciously controlled.

Layers of smooth muscle cells are found in the walls of the arteries, which are blood vessels that carry blood from the heart to the rest of the body. Smooth muscle α-2 actin contributes to the ability of these muscles to contract, which allows the arteries to maintain their shape instead of stretching out as blood is pumped through them.

Health Conditions Related to Genetic Changes

familial thoracic aortic aneurysm and dissection

More than 30 *ACTA2* gene mutations have been identified in people with familial thoracic aortic aneurysm and dissection (familial TAAD). This disorder involves problems with the aorta, which is the large blood vessel that distributes blood from the heart to the rest of the body. The aorta can weaken and stretch, causing a bulge in the blood vessel wall (an aneurysm). Stretching of the aorta may also lead to a sudden tearing of the layers in the aorta wall (aortic dissection). Aortic aneurysm and dissection can cause life-threatening internal bleeding.

ACTA2 gene mutations that are associated with familial TAAD change single protein building blocks (amino acids) in the smooth muscle α-2 actin protein. These changes likely affect the way the protein functions in smooth muscle contraction, interfering with the sarcomeres' ability to prevent arteries from stretching. The aorta, where the force of pumping blood coming directly from the heart is most intense, is particularly vulnerable to this stretching, resulting in the aortic aneurysms and dissections associated with familial TAAD.

other disorders

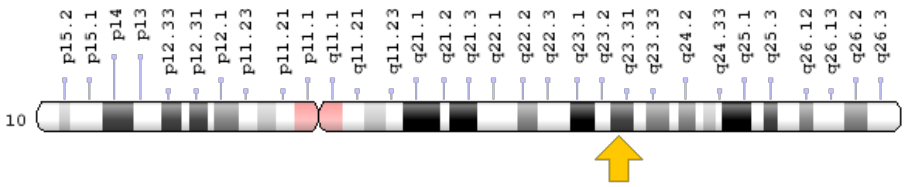
At least one mutation in the *ACTA2* gene causes multisystemic smooth muscle dysfunction syndrome. This disorder impairs the activity of smooth muscles throughout the body and leads to widespread problems including blood vessel abnormalities, decreased response of the pupils to light, a weak (hypotonic) bladder, and impairment of the muscle contractions that move food through the digestive tract (hypoperistalsis).

The mutation that causes multisystemic smooth muscle dysfunction syndrome replaces the amino acid arginine with the amino acid histidine at protein position 179, written as Arg179His or R179H. This mutation results in impaired contraction of smooth muscles in many organs, leading to the signs and symptoms of multisystemic smooth muscle dysfunction syndrome. It is unclear why this *ACTA2* gene mutation has effects on smooth muscles throughout the body while others affect only the aorta.

Chromosomal Location

Cytogenetic Location: 10q23.31, which is the long (q) arm of chromosome 10 at position 23.31

Molecular Location: base pairs 88,935,074 to 88,991,397 on chromosome 10 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- AAT6
- ACTA_HUMAN
- actin, aortic smooth muscle
- ACTSA
- alpha 2 actin
- alpha-actin-2

- cell growth-inhibiting gene 46 protein
- growth-inhibiting gene 46

Additional Information & Resources

GeneReviews

- Heritable Thoracic Aortic Disease Overview
  https://www.ncbi.nlm.nih.gov/books/NBK1120

Genetic Testing Registry

- GTR: Genetic tests for ACTA2
  https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=59%5Bgeneid%5D

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28ACTA2%5BTIAB%5D%29+OR+%28AAT6%5BTIAB%5D%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D

OMIM

- ACTIN, ALPHA-2, SMOOTH MUSCLE, AORTA
  http://omim.org/entry/102620
- MULTISYSTEMIC SMOOTH MUSCLE DYSFUNCTION SYNDROME
  http://omim.org/entry/613834

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/GC_ACTA2.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=ACTA2%5Bgene%5D
- HGNC Gene Family: Actins
  http://www.genenames.org/cgi-bin/genefamilies/set/929
- HGNC Gene Symbol Report
  http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=130
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/59
- UniProt
  http://www.uniprot.org/uniprot/P62736

Sources for This Summary

- OMIM: ACTIN, ALPHA-2, SMOOTH MUSCLE, AORTA
  http://omim.org/entry/102620
- El-Hamamsy I, Yacoub MH. Cellular and molecular mechanisms of thoracic aortic aneurysms. Nat Rev Cardiol. 2009 Dec;6(12):771-86. doi: 10.1038/nrcardio.2009.191. Epub 2009 Nov 3. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/19884902
- GeneReview: Heritable Thoracic Aortic Disease Overview
  https://www.ncbi.nlm.nih.gov/books/NBK1120
- Grond-Ginsbach C, Pjontek R, Aksay SS, Hyhlik-Dürr A, Böckler D, Gross-Weissmann ML. Spontaneous arterial dissection: phenotype and molecular pathogenesis. Cell Mol Life Sci. 2010 Jun;67(11):1799-815. doi: 10.1007/s00018-010-0276-z. Epub 2010 Feb 14. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/20155481
- Guo DC, Pannu H, Tran-Fadulu V, Papke CL, Yu RK, Avidan N, Bourgeois S, Estrera AL, Safi HJ, Sparks E, Amor D, Ades L, McConnell V, Willoughby CE, Abuelo D, Willing M, Lewis RA, Kim DH, Scherer S, Tung PP, Ahn C, Buja LM, Raman CS, Shete SS, Milewicz DM. Mutations in smooth muscle alpha-actin (ACTA2) lead to thoracic aortic aneurysms and dissections. Nat Genet. 2007 Dec;39(12):1488-93. Epub 2007 Nov 11. Erratum in: Nat Genet. 2008 Feb;40(2):255.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/17994018
- Jondeau G, Boileau C. Genetics of thoracic aortic aneurysms. Curr Atheroscler Rep. 2012 Jun; 14(3):219-26. doi: 10.1007/s11883-012-0241-4. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/22415348
- Milewicz DM, Carlson AA, Regalado ES. Genetic testing in aortic aneurysm disease: PRO. Cardiol Clin. 2010 May;28(2):191-7. doi: 10.1016/j.ccl.2010.01.017. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/20452526
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3615454/
- Milewicz DM, Guo DC, Tran-Fadulu V, Lafont AL, Papke CL, Inamoto S, Kwartler CS, Pannu H. Genetic basis of thoracic aortic aneurysms and dissections: focus on smooth muscle cell contractile dysfunction. Annu Rev Genomics Hum Genet. 2008;9:283-302. doi: 10.1146/annurev.genom.8.080706.092303. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/18544034
- Milewicz DM, Østergaard JR, Ala-Kokko LM, Khan N, Grange DK, Mendoza-Londono R, Bradley TJ, Olney AH, Adès L, Maher JF, Guo D, Buja LM, Kim D, Hyland JC, Regalado ES. De novo ACTA2 mutation causes a novel syndrome of multisystemic smooth muscle dysfunction. Am J Med Genet A. 2010 Oct;152A(10):2437-43. doi: 10.1002/ajmg.a.33657.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/20734336
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3573757/
- Morisaki H, Akutsu K, Ogino H, Kondo N, Yamanaka I, Tsutsumi Y, Yoshimuta T, Okajima T, Matsuda H, Minatoya K, Sasaki H, Tanaka H, Ishibashi-Ueda H, Morisaki T. Mutation of ACTA2 gene as an important cause of familial and nonfamilial nonsyndromatic thoracic aortic aneurysm and/or dissection (TAAD). Hum Mutat. 2009 Oct;30(10):1406-11. doi: 10.1002/humu.21081.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/19639654
- Pyeritz RE. Heritable thoracic aortic disorders. Curr Opin Cardiol. 2014 Jan;29(1):97-102. doi: 10.1097/HCO.0000000000000023. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/24284977

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